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(54) Title: KIT FOR CONTACT LENSES

(57) Abstract

The invention relates to a kit for treating contact lenses comprising a wetting and a cleaning composition. The wetting composition contains egg white lysozyme and enzyme activating tris(hydroxymethyl)aminomethane in addition to lacrophyl components. The pH value and surface tension is similar to the properties of natural tear. The cleaning composition contains urea and egg white lysozyme and lacrophyl components.

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KIT FOR CONTACT LENSES

The invention relates to kits for wetting and cleaning of contact lenses.

Replacement of tears were carried out for several decades by using tear substitutes in the form of arteficial tears. Efforts had been made to sooth the sensation of "dryness" of the eye in the case of insufficiency of tear production and at contact lens wear. Contact lens fitting and wetting solutions are employed all over the world.

An important recognition is that the tear covers the healthy cornea in form of a tear film consisting of 3 layers. The innermost layer of the 10 nm thick tear film consists mainly of mucin, the middle layer is an aqueous layer containing different organic and inorganic molecules, the outermost layer contiguous with the air is of lipid nature. In the last years the greatest attention has been drawn to the innermost layer adhesing to the cornea. A decisive role of the mucin layer has been implicated in the formation of the tear film. At the application of tear substitutes efforts had been made for the substitution of mucin. Originally the thickness of the mucin layer had been measured to be 0.02-0.05 nm, but according to recent measurings the thickness of the mucin layer can attain even 10 nm (Nichols et al: Invest. Ophthalmol. Vis. Sci. 26, 464-473, 1985). The tear fluid adheres to

the cornea uniformly. By the surface activity of mucin the tear fluid is not drop-shaped, but forms a three-layered film upon the cornea, one of the most important tissues regarding the optic of the eye.

The tear film ensures the physical, chemical and microbiological protection of the cornea. Hence one of the most important guarantee of vision if the uniform and constant tear film. In the last years it had been realized that besides the grave pathological dry eye conditions the contact lens wear is also a cause of dry eye (Ferris R.: CLAD journal 12, 234-246, 1986).
Contact lens wear spread all over the world for the correction of errors of refraction. Lenses produced from different synthetic materials can be grouped according to their physical properties fundamentally in three groups: hard lenses, oxygen permeable semi-hard lenses and soft lenses.

The use of contact lens wetting solutions are necessary while fitting or simply inserting hard contact lenses and for soaking of soft contact lenses, for proper wetness. Contact lens wetting solutions are also necessary for the prevention of the development of eye dryness (sicca syndrome). The right contact lens wetting solution should have a prophylactic defensive natur in prevention of the eye from the develop-

ment of the sicca syndrome.

The wetting solution should be supplemented by a cleaning solution which is free of toxic materials.

The tear substitutes and contact lens wetting solutions contain synthetic macromolecules for the substitution of mucin and to attain adequate viscosity. These "artificial tears" and contact lens wetting solutions are completed with preservatives to prevent bacterial contaminations, since solutions containing macromolecules (e.g. polyvinylalcohol, dextran etc.) become easily culture mediums for bacteria. They also easily obstruct the pores of the soft lenses. To prevent bacterial contaminations these solutions contain some preservatives, e.g. benzalkonium chloride, chlorbutanol or some mercury compounds, e.g. thiomersal. These compounds easily cause allergic reactions, moreover they are also toxic.

These facts need distinguished attention when contact lens wetting solutions are used. Contact lenses take up preservatives and by the interaction of these toxic compounds with the material of the lenses, they are concentrated by the lenses. The effective concentration of the preservatives at the surface of the contact lens is much higher than the concentration in the contact lens wetting solution. The toxic

effect is the greatest at the corneal epithelium, where the preservatives are released from the lens material.
Preservatives being lipophil compounds interact with the superficial lipid layer of the tear film. Mucin of the
tear film coats the lipophil preservatives linked to tear lipid and discharges them through the dacro-lachrymal system. Tear deficiency develops in the case of mucin consumption.

It is the aim all over the world to eliminate preservatives in the tear substitutes.

In addition to the contact lens wetting solutions contact lens cleaning solutions are of great importance, since visual acuity and integrity of the cornea depend on them. In case of the use of insufficient contact lens cleaning solutions deposits of contaminations might impede visiion, pores of contact lenses might be obstructed, by which oxygen supply of the cornea decreases and cornea metabolism might get impaired. In all three types of lenses (hard, soft and oxygen permeable lenses) deposits of contaminations might injure the cornea and might cause inflammation of the conjunctiva and the cornea, in many cases even before the appearance of visible contaminations. Life expectancy of the lenses is also dependent on the appropriate cleaning solution. While life expectancy of the hard lenses is of several years, soft lenses have life expectancy from one half a year to

one year. Reason of this is that cleaning of soft lenses is much more difficult than cleaning of hard lenses. Hence the wear of soft contact lenses is of a great expense than the wear of hard contact lenses.

The use of cleaning solutions of good quality enables the contact lens wearer with less danger and also the life expectancy of contact lenses can be elongated. By this means contact lens wear (all three types, soft, hard and oxygen permeable) becomes more economical.

Cleaning solutions can be grouped according to their application

a) disinfection solutions,
b) disinfection and storing solutions,
c) solutions for heat disinfection,
d) general cleaning solutions,
e) intensive cleaning solutions,
f) periodically used cleaning solutions,
g) cleaning solutions for daily use.

Grouping of cleaning solutions according to the chemical reactions involved in the cleaning procedure:

1) heat denaturation,
2) proteases,
3) peroxides and iodine,
4) mercury compounds,
5) benzalkonium chloride and chlorhexidine (Brewitt H. and Mandel S.: Contactologia 10D, 53-58, 1988),

6) silver compounds (Bonkhoff P.: Contactologia 10D, 59-66, 1988),
7) compounds which prevent adhesion of proteins to contact lenses (Cerulli et al: Contactologia 10D, 62-72, 1988).

Inspite of the many kinds of cleaning and disinfection possibilities of contact lenses being available, cleaning and disinfection are still a problem (Donzis P.B. et al: Am. J. Ophthalmol. 104, 325-333, 1987, Herve L. et al: Contactologia 10D, 151-154, 1988, Bisignano G. et al: Contactologia 10D, 155-158, 1988).

One object of the invention is to prepare a kit for the treatment of hard, semi-hard and soft contact lenses which have a composition similar to the composition of tear, by use of which kit the wetting and cleaning of the contact lenses can be effected. Another object of the invention is to decrease the number of manipulations necessary to use contact lenses and to eliminate the impairment (damage) of eye.

The kit suitable for treatment of contact lenses comprises a wetting and a cleaning composition and the wetting composition contains 0.1 to 1.0 weight% of lysozyme (egg white lysozyme EC 3.2.1.17),

0.02 to 10.0 weight% of ascorbic acid and/or 0.01 to 1.0 weight% of citric acid

0.18 to 3.6 weight% of tris(hydroxymethyl)aminomethane
0.05 to 1.0 weight% of boric acid and/or
0.05 to 0.1 weight% of ethylenediaminetetraacetic acid disodium salt
0.45 to 0.9 weight% of sodium chloride
99.4 to 83.4 weight% of distilled water

while the cleaning composition contains

0.1 to 1.0 weight% of lysozyme (egg white lysozyme EC 3.2.1.17)
3.0 to 12.0 weight% of urea
0.02 to 10.0 weight% of ascorbic acid and/or citric acid
0.18 to 3.6 weight% of tris(hydroxymethyl)aminomethane
0.05 to 1.0 weight% of boric acid and/or
0.05 to 0.1 weight% ethylenediaminetetraacetic acid disodium salt
0.45 to 0.9 weight% of sodium chloride
96.0 to 71.4 weight% of distilled water.

The wetting composition has a pH value of 6.8 which is adjusted by means of tris(hydroxymethyl)-aminomethane.

A preferred wetting composition contains 0.1 weight% of chicken egg white lysozyme, 1.8 weight% of tris(hydroxymethyl)aminomethane, 0.5 weight% of boric acid, 0.5 weight% of ascorbic acid, 0.45 weight% of sodium chloride in solution prepared with distilled water.

Another preferred wetting composition contains

0.1 weight% of egg white lysozyme HCl,
2.7 weight% of tris(hydroxymethyl)aminomethane,
0.5 weight% of boric acid,
1.64 weight% of citric acid,
0.1 weight% of ethylenediaminetetraacetic acid disodium salt.

The lysozyme activity of the wetting compositions is 18.500 U/ml (determination of activity according to Shugar, D: Biochim. Biophys. Acta 8, 302, 1952).

The surface activity of the wetting composition is 45-50 dyn cm^{-1} (measured by means of Du Nouy tensiometer).

A preferred cleaning composition contains 3 weight% of urea, 0.1 weight% of egg white lysozyme, 2.7 weight% of tris(hydroxymethyl)aminomethane, 0.5 weight% of boric acid, 1.64 weight% of citric acid, 0.1 weight% of ethylenediaminetetra-acetic acid sodium salt.

Another preferred cleaning composition contains 12 weight% of urea, 0.1 weight% of egg white lysozyme, 0.45 weight% of sodium chloride, 1.8 weight% of tris(hydroxymethyl)aminomethane, 1.6 weight% of citric acid, 0.5 weight% of boric acid and 0.05 weight% of ethylenediamine tetraacetic acid disodium salt.

The quality of the components equals to the

purity required by the pharmaceutical compositions. The lysozyme-HCl (mucopeptide N-acetyl muramoyl hydrolase, EC 3.2.1.17 quality (Worthington product, Free Ltd., New Jersey, USA)).

On preparing the compositions the tris(hydroxymethyl)aminomethane, the boric acid, the citric acid and the ethylenediaminotetraacetic acid disodium salt are dissolved in freshly distilled ion free water. The pH value of the solution is adjusted to 6.0 to 6.5. Thereafter the lysozyme HCl is added to the solution and after the dissolution thereof the pH value of the solution is adjusted to 6.8 by means of tris(hydroxymethyl)aminomethane and finally the solution is completed with distilled water to the end volume. The solution is left standing, the substances precipitated are removed by sterile filtration, then the sterilized solution is filled into the container, the composition is clear, turbidity free and has the required lysozyme activity.

It has been found that applying a lysozyme (muramidase, N-acetylmuramyl beta/1-4/ glycanohydrolase, EC 3.2.1.17) the tear film could advantageously be re-established similar to the effect of mucin. The role and effect of tear lysozyme could be achieved by applying its isoenzyme. A sufficient effect could be gained by employing an isoenzyme of tear lysozyme e.g. chicken egg white lysozyme. This is capable to form linkages with mucin which broadens

the innermost layer of the tear film and regulate surface tension. By this fact tear "break up time" ("BUT") characteristic for tear film stability becomes also appropriate. (Surface tension of the composition is 49 dyn. cm^{-1}, mean of surface tension of tears of healthy subjects is 41 dyn. cm^{-1} (Holly F. et al.: Exp. Eye Res. 24, 479-491, 1977)). It should be emphasized that this very advantageous surface tension is formed without preservatives, which being of lipid nature (but are toxic!) would lower the surface tension, in fact they lower the surface tension of the commercially available wetting compositions (arteficial tears) /Lemp M.A. and Holly F.: Ann. Ophthalmol. 15-20, 1972/. Relative viscosity of the tear substitute and contact lens wetting solution is low (1.07 referring to water) compared to the commercially available arteficial tear solutions and contact lens wetting solutions, containing synthetic macromolecules. Inspite of it, it has advantageous absorbtive properties on the corneal epithelium.

The tris(hydroxymethyl)aminomethane used for the dissolution of lysozyme and for the regulation of the pH and of the osmosis pressure of the solution, gives unexpectedly a significant enzyme activity enhancing effect.

Remarkable results can be achieved by using lysozyme solutions with ascorbic acid and/or citric acid additives. Antiphlogistic and collagenase inhibiting effect of lysozyme is advantageously completed by them. Ascorbic

acid and citric acid are also known for their antiphlogistic nature, hence by using the compositions containing lysozyme with ascorbic acid and/or citric acid the synergetic action resulted in a significant antiphlogistic effect. The good therapeutic effect is supplemented by hemostatic, analgetic and antihistamin properties.

By the most important effect of lysozyme, the bacteriostatic effect - not merely the eye is protected against infection - but the solution itself is also protected against microbiological contaminations. The use of preservatives is either totally superfluous, or it is needed only to a very little extent. For this purpose boric acid proved useful. Also the use in some cases of ethylenediaminetetraacetic acid proved to be satisfactory.

The compositions of the invention dispose important microbiological defense mechanism. According to the investigations they display significant bacteriostatic effects against the most dangerous Gram positive and Gram negative bacteria strains to the eye, e.g. Staphylococcus aureus and Pseudomonas aerugonosa (2.10^6 cells/ml within 4 hours).

The wetting composition may be used in addition for the following purposes:
In the "dry-eye" syndrome (developed during ageing, or in connection or consequence of some disease, or appearing as a side-effect of

medical treatment) as eye-drop solution;
after cataract surgery and artificial lens implantation, for the treatment of bacterial and allergic conjunctivitis, herpes virus, adenovirus or other infective diseases, collagen diseases of the cornea, inflammatory or malign processes of the eye-lid as eye-drop solution or lotion.

Similar to the composition of the contact lens wetting solution, the composition for cleaning of hard, soft and oxygen permeable semihard contact lenses should be harmless to the cornea and should contain mainly lacrophil natural compounds.

Contaminations of contact lenses can be prevented when adding urea to the wetting composition. By increasing the amount of urea a definite cleaning effect has been achieved. By increasing the amount of urea from 0.05 M to 0.5 M - 2.0 M the cleaning effect can be increased also.

Accordingly the main compounds of the contact lens cleaning solution are urea and chicken egg white lysozyme (muramidase, N-acetyl-muramyl/1-4/ glycanohydrolase EC 3.2.1.17).

The lysozyme enhances the aggregation of bacteria such as Staphylococcus aureus and thus inhibits the adherence thereof to the contact lens.

The contact lens cleaning composition contains

beside the above mentioned compounds tris(hydroxy-methyl)aminomethane (TRIS), which acts as a pH regulator and enzyme activator, citric acid, which exerts favourable effects on protein structure and boric acid and ethylenediaminetetraacetic acid disodium (EDTA Na_2) which synergetically increase the bacteriostatic effect of the composition. Concentrations of all components are similar to that of the contact lens wetting composition. Great advantage of the cleaning composition is that most of the components are also present in the natural tear fluid. The natural tear fluid also contains urea, though in a much smaller concentration (0.03-0.05%). Lysozyme content of tears is about the same as that of the contact lens wetting solution. A subsequent use of the cleaning and wetting solution is possible, because rinsing the contact lens with the wetting solution thoroughly, it can be directly inserted into the eye.

By applying urea to the cleaning solution a decrease of manipulations, on the use of contact lenses can be achieved and also the errors of manipulations could be decreased, thereby the protection of the cornea can be attained with great security.

The cleaning solution can be employed as a general cleaning solution, as a periodical cleaning solution or as a daily cleaning solution.

As it is to be seen from the above description, two compositions are necessary for the wear

of contact lenses from which no one contains preservatives. The two compositions form a "kit" for contact lens wearer. The contact lens wearer inserts the contact lenses (in case of hard lenses with 3-4 drops in case of soft contact lenses immerses his contact lenses for soaking) with the contact lens wetting solution into the eyes. Should the contact lens wearer feel the eyes "dry" during contact lens wear, a few drops of the contact lens wetting composition suffice to comfort the eyes. "Dryness" feeling ceases and by this contact lens wetting solution works also as a lubricating and rewetting solution.

The cleaning effect of the contact lens cleaning composition is of such a degree, that immersing contact lenses (soft, hard or oxygen permeable semihard lenses) into the contact lens cleaning composition for 4-5 hours, contaminations can be simply shaken off, without rubbing. So contact lenses are spared to a high degree, and they can be removed from the cleaning composition without a scratch.

The Examples illustrate the details of the invention without restricting its scope:

Example 1

egg white lysozyme	0.10 %
sodium chloride	0.45 %
tris(hydroxymethyl)aminomethane (TRIS)	1.80 %
borid acid	0.50 %
ascorbic acid	0.50 %

in aqueous solution (sterile distilled water). This composition is suitable as a tear substitute and/or as a contact lens wetting composition.

Example 2

Tear substitute and contact lens wetting composition:

chicken egg white lysozyme. HCl	0.1 %
TRIS	2.7 %
boric acid	0.5 %
citric acid	1.64%
ethylenediaminetetraacetic acid disodium salt (EDTA-Na_2)	0.1 %

in aqueous solution (sterile distilled water).

Preparation of 40 l contact lens wetting composition:

1080 g of TRIS, 200 g of boric acid, 656 g of citric acid and 40 g of EDTA-Na_2 are dissolved in 32 l of distilled water. The dissolution can be completed by stirring, but every single component should be added in the given sequence. Thereafter pH should be adjusted to pH 6.0-6.5 with 3 M TRIS. 40 g lysozyme.HCl should be put on the top of the solution. Lysozyme dissolves without stirring. After complete dissolution the pH should be adjusted to pH = 6.8 with TRIS. Sterilization should be performed by filtration through a bacterium filter in a sterile system.

Physico-chemical properties of the contact lens wetting composition:

pH	6.8
osmolarity	300 mOzmol
surface tension	49 $dyn.cm^{-1}$
relative viscosity (in relation to water)	1.07
lysozyme activity	18.500 U/ml

(Analytical method according to Shugar, D.: Biochim. Biophys. Acta 8, 302, 1952)

Lysozyme activity measurings were repeated after storage at $4^{o}C$ for 14 month: lysozyme activity proved to be 18.500 U/ml.

Clinical tests:

In a double blind study 25 dry patients were treated with the wetting composition (Example 2) for two weeks. After two weeks interval the same patients were treated with a tear substitute containing synthetic macromolecules. 17 patients recommended the lysozyme containing composition for better, 7 patients qualified the two tear substitutes for equally good. No itching, stingig or allergic reactions had been registered. Schirmer and BUT values improved in all 25 patients. By using the wetting composition (Example 2) in only 4 of the 25 patients Rose Bengal staining of the cornea remained slightly positive.

Example 3

Contact lens wetting composition.

Dry ampolue:

chicken egg white lysozyme	0.01	g
ascorbic acid	0.02	g
(in a separate dissolving capsule)		

Dissolving ampoule or eye-drop bottle:

10 ml aqueous solution of sodium chloride	0.45	%
TRIS	1.8	%
boric acid	0.5	%

Content of the dry ampoule is to be dissolved in the content of the dissolving ampoule (eye-drop bottle). pH of the solution is 7.3. Dry ampoule and dissolving ampoule (eye-drop bottle) can be stored separately for years.

Example 4

Contact lens wetting composition:

chicken egg white lysozyme	0.1	%
sodium chloride	0.3	%
TRIS	2.4	%
boric acid	0.05	%
citric acid	0.88	%

In aqueous solution (sterile bidistilled water) physico chemical properties:

pH	7.1
osmolarity	305 mOzmol
surface tension	46.8 $dyn.cm^{-1}$
relative viscosity	1.07

Example 5

Contact lens wetting composition:

chicken egg white lysozyme	1.0 %
sodium chloride	0.45 %
TRIS	1.8 %
ascorbic acid	2.0 %
ethylenediamine tetraacetic acid di-sodium (EDTA Na_2)	0.05 %

in aqueous solution (sterile bidistilled water) pH of the solution: pH = 6.7

Example 6

Contact lens cleaning composition:

urea	3.0 %
egg white lysozyme	0.1 %
TRIS	2.7 %
boric acid	0.5 %
citric acid	1.64 %
EDTA-Na_2	0.1 %

in aqueous solution, pH of the solution is adjusted to pH = 6.8 with TRIS.

Contaminations of contact lenses (hard, soft and oxygen permeable semi-hard lenses) are cleaned with mild rubbing after 4-5 hours immersing in the solution.

A several years' trial of an ophthalmologist prescribing and fitting hard, semihard and gas-permeable contact lenses since 50 years proved comfort feeling and decrease of yearly irritation

symptoms, when using lysozyme containing contact lens wetting and storage solutions (Example 2) and contact lens cleaning solution (Example 6). The cleaning solution especially worked well by decreasing the inconvenient "greasiness" phenomenon.

Example 7

Contact lens cleaning composition:

urea	9.0 %
egg white lysozyme	0.1 %
TRIS	2.7 %
citric acid	1.64%
boric acid	0.5 %
EDTA-Na_2	0.1 %

in aqueous solution. pH of the solution is adjusted to pH = 6.8. The solution can be employed for immersing contact lenses (soft, hard, oxygen permeable semihard contact lenses) for 5-6 hours. Contaminations can be removed by mere shaking off.

Preparation of 40 l contact lens cleaning solution:

The process is similar to the preparation of the acontact lens wetting and storage solution (see Example 2), but 3600 g (9 %) urea is dissolved just before lysozyme is added.

Physicochemical properties of the contact lens cleaning solution:

pH	6.8		
lysozyme activity	15.500 U/ml		
density	1.0642	g/ml	25°C

According to microbiological investigations the contact lens cleaning solution has a proper bacteriostatic activity against the most important bacteria (Staphylococcus aureus, Escherichia coli and Pseudomonas aeruginosa) within the 72 hours examination, even if it is twice diluted.

To prove the advantage of the wetting and storage solution and to assess the cleaning capacity of the cleaning solution complex studies both in vitro and in vivo have been performed. After determining the length of time necessary for cleaning (which proved to be about 3 - 3 1/2 hours) and not to jeopardize the eye and for the sake of soundness of the contact lens well the time for removing urea absorbed by the contact lens had to be determined. From studies in vitro in became clear that the span of time for cleaning and the subsequent soaking in physiological saline or in the wetting solution for the removal of urea proved to be equally about 3 - 3 1/2 hours

In vivo studies for three months has been performed with soft contact lens wearing patients using the lysozyme containing contact lens wetting and storage solution (20 eyes). A comparison of the lysozyme containing cleaning solution with a protein remover (Bausch and Lomb) has been performed.
Group A of soft lenses wearing patients used once a week the lysozyme containing contact lens cleaning lens cleaning solution for 6 hours.

After thorough rinsing with physiological saline, inserted their lenses in physiological saline for another 6 hours. The lenses were stored in the Lacrozym wetting and storage solution. Group B of soft lenses wearing patients used the lysozyme containing wetting and storage solution similar to patients of group A, but used for cleaning of contact lenses a protein remover (Bausch and Lomb). Thereafter the lenses were stored in the lysozyme containing wetting and storage solution.

Patients in both groups feeled the solutions for comfortable and easy to handle. Moreover they felt especially useful to apply the wetting solution as eye-drops during the day while wearing the contact lenses. This proved to lengthen wearing time, hence it worked as an in-eye-lens lubricant very advantageously. Lysozyme containing cleaning solution and Bausch and Lomb protein remover proved to be equally effective even in long term use. So even the periodical use of a protein remover -recommended by most of the commercially available contact lens cleaner can be eliminated. By this the risk to have traces of protease residues left on the lenses ceases.

Exmaple 8

Contact lens cleaning composition:

urea	12.0 %
egg white lysozyme	0.1 %
sodium chloride	0.45 %

TRIS	1.8	%
citric acid	1.64	%
boric acid	0.5	%
EDTA-Na_2	0.05	%

in aqueous solution. pH of the solution is adjusted to pH = 6.8.

C l a i m s

1. A kit suitable for treatment of contact lenses comprising a wetting and a cleaning composition wherein the wetting composition contains
0.1 to 1.0 weight% of lysozyme (egg white lysozyme EC 3.2.1.17),
0.02 to 10.0 weight% of ascorbic acid and/or
0.01 to 1.0 weight% of citric acid,
0.18 to 3.6 weight% of tris(hydroxymethyl)aminomethane,
0.05 to 1.0 weight% boric acid and/or
0.05 to 1.0 weight% of ethylenediaminetetraacetic acid disodium salt
0.45 to 0.9 weight% of sodium chloride,
99.4 to 83.4 weight% of distilled water,

while the cleaning composition contains

0.1 to 1.0 weight% of lysozyme (egg white lysozyme EC 3.2.1.17),
3.0 to 12.0 weight% of urea,
0.02 to 10.0 weight% of ascorbic acid and/or citric acid,
0.18 to 3.6 weight% of tris(hydroxymethyl)aminomethane,
0.05 to 1.0 weight% of boric acid and/or
0.05 to 1.0 weight% ethylenediaminetetraacetic acid disodium salt
0.45 to 0.9 weight% of sodium chloride,
96.0 to 71.4 weight% of distilled water.

2. A composition according to claim 1 wherein

the wetting composition has a pH value of 6.8 adjusted by means of tris(hydroxymethyl)aminomethane.

3. A composition according to claim 1 wherein the wetting composition contains
0.1 weight% of egg white lysozyme,
1.8 weight% of tris(hydroxymethyl)aminomethane,
0.5 weight% of boric acid,
0.5 weight% of ascorbic acid,
0.45 weight% of sodium chloride.

4. A composition according to claim 1 wherein the wetting composition contains
0.1 weight% of egg white lysozyme.HCl,
2.7 weight% of tris(hydroxymethyl)aminomethane,
0.5 weight% of boric acid,
1.64 weight% of citric acid,
0.1 weight% of ethylenediaminetetraacetic acid disodium salt.

5. A composition according to claim 1 wherein the lysozyme activity of the wetting compositions is 18.500 U/ml.

6. A composition according to claim 1 wherein the cleaning composition contains
3 weight% of urea,
0.1 weight% of egg white lysozyme,
2.7 weight% of tris(hydroxymethyl)aminomethane,
0.5 weight% of boric acid,
1.64 weight% of citric acid,
0.1 weight% of ethylenediaminetetraacetic acid disodium salt.

7. A composition according toclaim 1 wherein the cleaning composition contains
12 weight% urea,
0.1 % of egg white lysozyme,
0.45 weight% of sodium chloride,
1.8 weight% of tris(hydroxymethyl)aminomethane,
1.6 weight% of citric acid,
0.5 weight% of boric acid and
0.05 weight% of ethylenediamine tetraacetic acid disodium salt.

INTERNATIONAL SEARCH REPORT

International Application No PCT/HU 91/00016

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) [6]

According to International Patent Classification (IPC) or to both National Classification and IPC

Int.Cl.[5]: G 02 C 13/00, A 61 L 2/18

II. FIELDS SEARCHED

Minimum Documentation Searched [7]

Classification System	Classification Symbols
Int.Cl.[5]	A 01 N 63/00, A 61 L 2/18, G 02 C 13/00

Documentation Searched other than Minimum Documentation to the Extent that such Documents are included in the Fields Searched [8]

III. DOCUMENTS CONSIDERED TO BE RELEVANT [9]

Category [10]	Citation of Document, [11] with indication, where appropriate, of the relevant passages [12]	Relevant to Claim No. [13]
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A	US, A, 4 355 022 (RABUSSAY) 19 October 1982 (19.10.82), see column 2, line 28 - column 5, line 12.	1,6,7
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* Special categories of cited documents: [10]

"A" *document defining the general state of the art which is not considered to be of particular relevance*

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"X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to *involve an inventive step*

"Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.

"&" document member of the same patent family

IV. CERTIFICATION

Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report
25 July 1991 (25.07.91)	31 July 1991 (31.07.91)
International Searching Authority	**Signature of Authorized Officer**
AUSTRIAN PATENT OFFICE	

Form PCT/ISA/210 (second sheet) (January 1985)

Anhang zum internationalen Recherchenbericht über die internationale Patentanmeldung Nr.

Annex to the International Search Report on International Patent Application No. PCT/HU 91/00016

Annexe au rapport de recherche internationale relatif à la demande de brevet international n°.

In diesem Anhang sind die Mitglieder der Patentfamilien der im obengenannten internationalen Recherchenbericht angeführten Patentdokumente angegeben. Diese Angaben dienen nur zur Unterrichtung und erfolgen ohne Gewähr.

This Annex lists the patent family members relating to the patent documents cited in the above-mentioned International search report. The Austrian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

La présente annexe indique les membres de la famille de brevets relatifs aux documents de brevets cités dans le rapport de recherche internationale visé ci-dessus. Les *renseignements fournis* sont donnés à titre indicatif et n'engagent pas la responsabilité de l'Office autrichien des brevets.

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